REMARKS

Claims 1-4, 7, 8, 12-16, 18, 19, 26-28, 50, and 53-70 are pending. Claim 14 is amended merely to correct a typographical error. The amendment raises no issues of new matter.

Rejections under 103(a)

Claims 1-4, 7, 8, 12-16, 18, 19, 26-28, 50, and 53-70 are rejected as being allegedly obvious over Crumb et al., U.S. Patent No. 6,030,943 ("Crumb") in view of Bobee et al., U.S. Patent No. 5,438,072 ("Bobee"). Without acquiescing in any way to the substance of the rejection, Applicants respectfully submit that the rejection should be withdrawn because Crumb is not available as a prior art reference, as detailed in the Declaration of Prior Invention under 37 CFR 1.131 ("Dr. Nuijen Declaration"), submitted herewith and executed by Dr. Bastisan Nuijen, an inventor on the instant application.

Applicants respectfully point out that Crumb qualifies as prior art only under 35 USC 102(e). Crumb has a non-provisional filing date of May 6, 1998, a provisional filing date of May 7, 1997, based on US Provisional Patent Application No. 60/045,803, and a publication date of February 29, 2000 (the issue date of the patent). The instant application enjoys an international filing date of February 18, 1999, and a foreign priority date of February 18, 1998, based on GB Patent Application No. 9803448.1. Thus, Crumb may have a prior art date under 35 USC 102(e) of May 7, 1997.

Nonetheless, the invention of the subject matter of the instantly-rejected claims was reduced to practice by at least before May 7, 1997, as detailed in Dr. Nuijen's Declaration and evidenced in the supporting exhibits. Specifically, Exhibit B, dated before May 7, 1997, and entitled "Interim Report of the Pre-Formulation Study of Aplidine (DDB)", evidences a reduction to practice of the invention according to currently-pending independent claims 1 and 12. Exhibit B describes the formulation of a lyophilized didemnin preparation comprising a didemnin compound (Aplidine) and a water-soluble material (mannitol) that is reconstituted using mixed solvents, namely, water for injection, an alkanol (ethanol), and a nonionic surfactant (propylene glycol or Cremophor EL), where the reconstitution provides a parenterally suitable

preparation, in accordance with pending claim 1. Exhibit B likewise discloses a reconstituted pharmaceutical composition comprising a didemnin compound (Aplidine); a water soluble material (mannitol); a nonionic surfactant (propylene glycol or Cremophor EL); an alkanol (ethanol); and water for injection; wherein the water for injection is present in an amount sufficient to allow solubilization of the water soluble material, and the alkanol is present in an amount sufficient to allow solubilization of the didemnin compound, in accordance with pending claim 12. Specific disclosures evidencing actual reduction to practice of the inventions of claims 1 and 12 can be found in Exhibit B, as outlined in the Table below:

Claim 1	**Claim 12**	**Actual Reduction to Practice as evidenced in Exhibit B**
a lyophilized didemnin preparation [which] comprises a didemnin compound and a water-soluble material	a didemnin compound; a water soluble material	The Aplidine (DDB) solution to be freeze-dried is composed of Alplidine (DDB) and mannitol (Table 5, page 8)
a reconstitution solution of mixed solvents [which] comprises water for injection, an alkanol, and a nonionic surfactant	a nonionic surfactant; an alkanol; and water for injection	The Aplidine (DDB) freeze-dried product dissolves in a propylene glycol/ethanol/ water for injection co-solvent system (Table 6, page 9) Cremophor EL/Ethanol is listed as an alternative formulation (Conclusion, page 11)
the water for injection is present in an amount sufficient to allow solubilization of the water soluble material	the water for injection is present in an amount sufficient to allow solubilization of the water soluble material	The Aplidine (DDB) freeze-dried product dissolves in a propylene glycol/ethanol/ water for injection co-solvent system (Table 6, page 9) Cremophor EL/Ethanol is listed as an alternative formulation (Conclusion, page 11)

the alkanol is present in an amount sufficient to allow solubilization of the didemnin compound	the alkanol is present in an amount sufficient to allow solubilization of the didemnin compound	The Aplidine (DDB) freeze-dried product dissolves in a propylene glycol/ethanol/ water for injection co-solvent system (Table 6, page 9) Cremophor EL/Ethanol is listed as an alternative formulation (Conclusion, page 11)
reconstitution of the lyophilized didemnin preparation with the reconstitution solution of mixed solvents provides a parenterally suitable preparation.		The freeze-dried product can be re-constituted shortly before administration to the patient (page 6)

Accordingly, the invention of the instant claims was actually reduced to practice by at least before May 7, 1997. This actual reduction to practice, Applicants respectfully point out, establishes invention of the instantly-claimed subject matter prior that date, the earliest potential effective filing date of Crumb, and thereby removes Crumb as a prior art reference.

Additional laboratory notebook entries from Dr. Nuijen's lab further corroborate this actual reduction to practice (see Exhibits C, D, and E and Dr. Nuijen's Declaration). In brief, the concept of using a mixed solvent system for reconstituting didemnin preparations is reported on in a laboratory notebook entry (Exhibit C) dated less than about one month prior to the actual reduction to practice reported in the Interim Report. The suitability of various mixed solvent systems composed of a nonionic surfactant, an alkanol, and water are described in an entry (Exhibit D) dated a little more than about one month following the actual reduction to practice reported in the Interim Report. Further, an entry dated May 7, 1997 (Exhibit E) reports on the suitability of reconstituting lyophilized didemnin preparations (including freeze-dried Aplidine and freeze-dried mannitol) using mixed solvent systems composed of an nonionic surfactant (Cremophor EL), an alkanol (ethanol), and water.

Having "sworn behind" the Crumb reference, Applicants respectfully submit that Crumb cannot be relied on to allegedly render obvious the invention of the instant application, neither alone nor in combination with any other reference. Accordingly, Applicants respectfully and earnestly request withdrawal of the 103(a) rejections directed at the currently-pending claims, and further respectfully note that there are no other outstanding rejections directed at the subject claims.

CONCLUSION

Applicants respectfully request entry of the above amendment and remarks and earnestly and respectfully request timely allowance of the subject claims. If a telephone call would help expedite any aspect of the prosecution of the instant application, Applicants encourage the Examiner to contact the undersigned to discuss same.

AUTHORIZATION

The Commissioner is hereby authorized to charge any fees which may be required for consideration of this paper to Deposit Account No. **50-3732**, Order No. 13566.105049. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time, or credit any overpayment, to Deposit Account No. **50-3732**, Order No. 13566.105049.

Respectfully submitted,
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Dated: November 9, 2010

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